A RELIABLE PARTNER IN DRUG DISCOVERY & TRANSLATIONAL MEDICINE

创新药物研发与转化医学的伙伴：中国医药城小分子药物研发中心

Ming Guo, Ph.D. 郭明博士

The Big Picture

Scientific Innovation

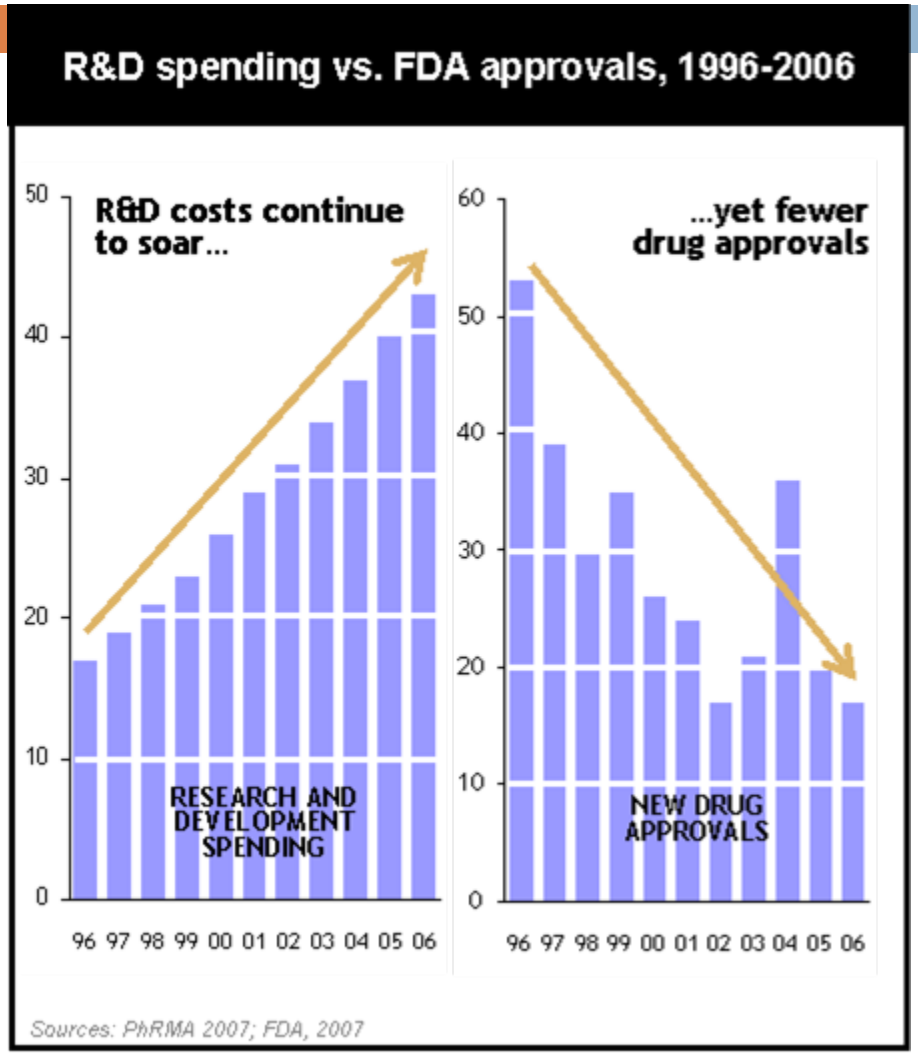
US: Always a driving force for US economy but negatively impacted by the 2008 global crisis

China: Historic turning point from “Made in China” to “Invent in China” against the global trend

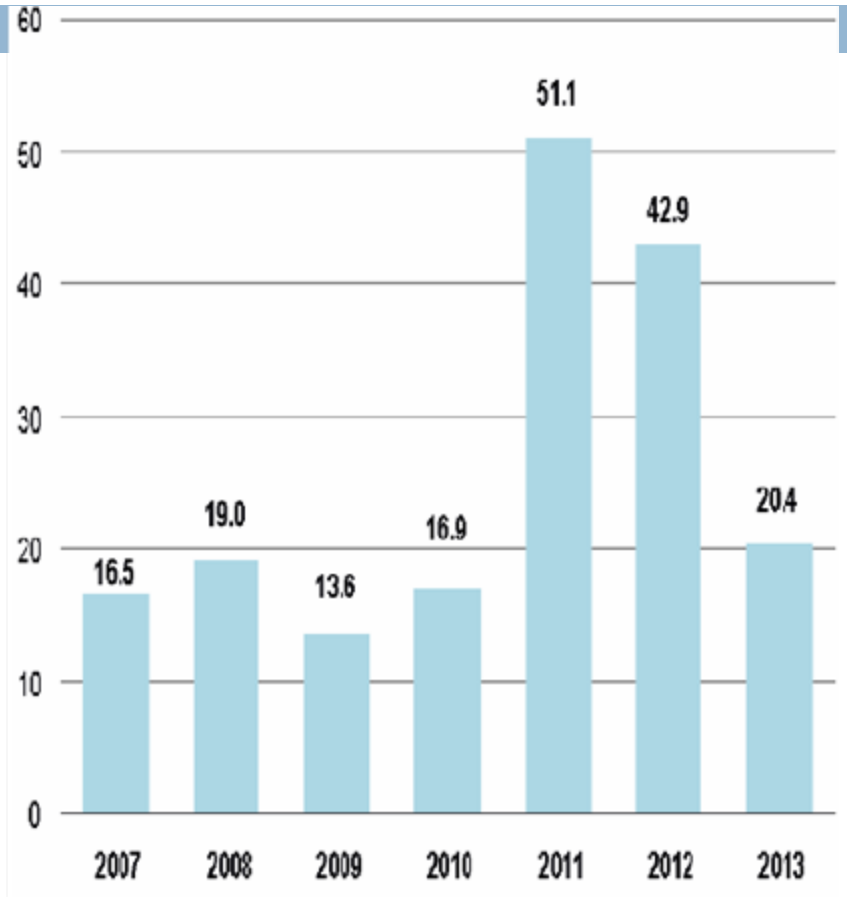
BioPharma Industry

Closely following the general trend

R&D Productivity Declining
Costs up / Approvals Down



Patent Expiry Tsunami Looms
$Bn's Lost to Patent Expiries[1]



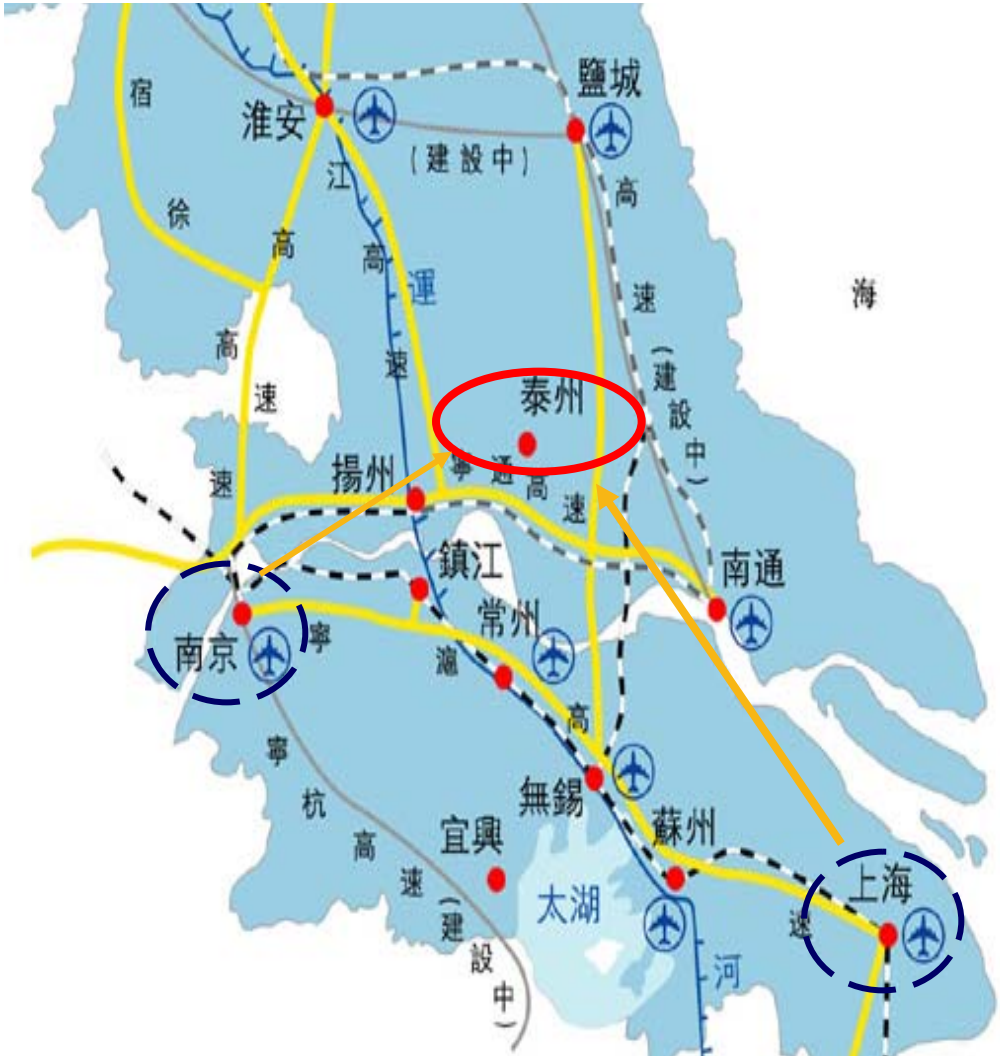
Source: EvaluatePharma

1 Includes Abbott, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, J&J, Merck, Novartis, Pfizer, Roche, Sanofi, Schering-Plough, and Wyeth. Revenue lost calculated as last full year of estimated sales prior to normally scheduled expiration

A Possible Path for China BioPharma R&D

- Healthy ROI needed for any valid industry
- Historical value Creation by biotech Industry
  - Saving Lives: Revolutionary drugs for un-med medical needs; but marginal innovation valuable for local patients at this point
  - "Show me the money":
    - Investors / Shareholders Return – Genentech vs. Pfizer on the day of its sale to Roche (2009-3-26) at $95 per share for $100 B market cap (> PFE)
    - P/E ratio (1-yr forward) > 4x of that for Big Pharma (> 130 in 1999)
    - WX IPO Aug 2007 – Share price x2 (to $40) in 5-6 weeks with the high P/E ratio (ca. 40) for > $2 B market cap
    - Hutchinson MediPharma out licensing Nov. 2011 – $20 M upfront / $120 M total
- Lessons for China NCE drug R&D by biotech co's
  - Several significant financial milestones needed as the catalyst
  - Scientific achievement plus "China concept" for business success
  - Mentality shift: it does not always take a commercial stage product to make money

China Medical City



Location: Taizhou

- Located at the center of Jiangsu province within the Yangtze River Delta
- 2.5 hrs north of Shanghai
- 1.5 hrs east of Nanjing
- Yangzhou-Taizhou Airport (May 8, 2012) and high speed train (in *ca*. a year)

CMC Overview

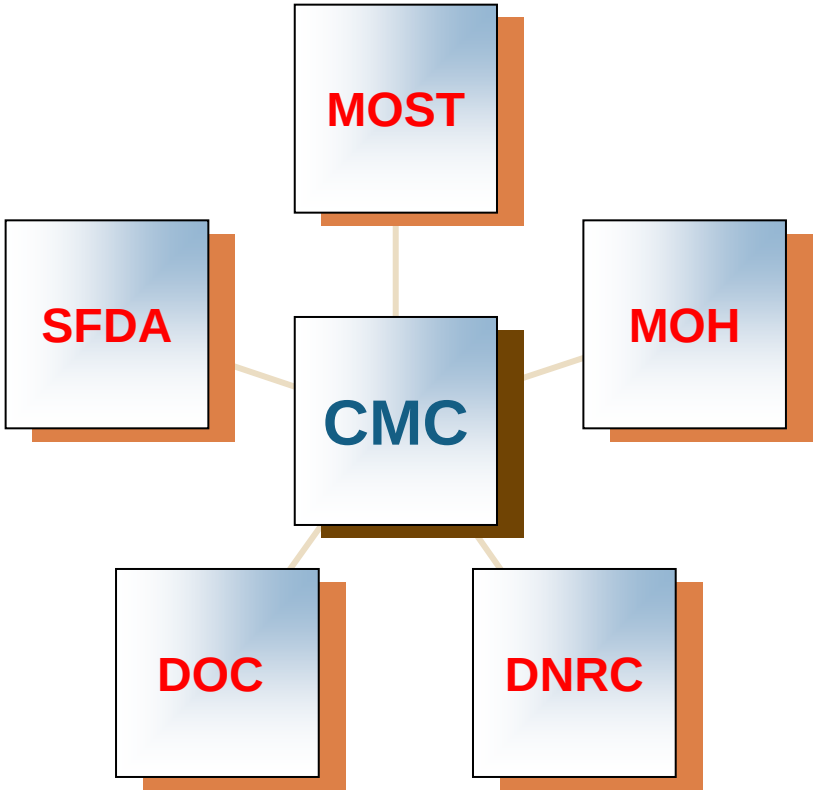
CMC 中国医药城 China Medical City

泰州国家医药
高新技术产业开发区
Taizhou National Medical Hi-tech Development Zone

• CMC is the only state level bio medical development zone, with a total area of 30 square kilometers.

• The city is divided into six functional districts: R&D, Manufacture, Exhibition, Healthcare service, Education, Residential & Commercial districts.

State and Local Level Advantages



- Direct support from four ministries to work together
- Direct communication between regulatory authority and site for innovation projects
- Aiming to make CMC the “ the leader in China as a world-class life science cluster”
- CMC venture fund for financial support to the localized innovation projects

R&D Centers / Platforms

R&D District: One of the 6 districts at CMC to collaborate with universities, research institutes and to incubate innovative technologies and products

Development platforms: small molecules, biologics, vaccine and diagnostics, etc.

Small Molecule Drug R&D Center: to assist transformation of the Chinese pharmaceuticals into an innovation based industry (2 floors; ca. 6000 m2)

Small Molecule Drug R&D Center

中国医药城 China Medical City

泰州国家医药高新技术产业开发区
Taizhou National Medical Hi-tech Development Zone

- Current Focus
  - Late stage discovery support
  - Translational medicine
  - IND enabling and application, through POC stages
- Open to any form of collaboration and/or services, including
  - Open access to its instruments and facilities,
  - Fee-for-service projects,
  - Integrated IND package for SFDA and FDA,
  - Risk sharing projects,
  - Incubator function, etc.
- Potential collaboration partners include
  - Research companies,
  - Virtue companies,
  - Entrepreneurs and entrepreneurs-to-be
  - Established domestic companies and global companies aiming at reliable translational medicine partner and/or IND registration with SFDA and/or FDA.

Managing Company: Ascentage

- A 2009 spin-off company from Ascenta (Shanghai) R&D Center, to capitalize on its leading position and track record in global NCE drug R&D
- Registered as a Jiangsu company in Taizhou (2010) and entered into the collaboration agreement with CMC to establish and manage the Small Molecule R&D Center in 2011
- Proven Global Track Record
  - One of the first US NCE drug companies entering China (2005)
  - Experienced executive team covering all critical aspects
  - A stable team of scientists trained according to the US standards
  - Successful global IND filing record (FDA and SFDA) for NCE drugs

小分子药物研发中心：药学（CMC）

- 合成化学
  - 合成关键砌块
  - 合成临床候选药物筛选所需的后期类似物库
  - 合成生物学研究所需的临床候选药物
  - 临床候选药物盐形-晶形的研究和筛选

- 工艺化学
  - 药物化学路线的放大制备和评估
  - 工艺优化
  - 为毒理研究提供公斤级药物
  - 生产工艺技术包的开发和转移

小分子药物研发中心：药学（CMC）

- 分析方法开发与验证

  按照中/美两国药典要求进行HPLC\GC\LC-MS等分析方法的开发与验证

- 杂质与杂质谱研究

- GMP分析服务
  - 具有相应的实验室质量管理规范
  - 具有相应的质量检验标准操作规程
  - 经验丰富的分析方法技术转移与验证

小分子药物研发中心：药学（CMC）

- 处方前研究
  - 药物形态学研究与确认
  - 药物理化性质研究
  - 药物与辅料相容性研究
- 制剂开发
  - 新药制剂开发
  - 缓控释制剂开发
  - 固体分散技术制剂开发
- 稳定性测试
  - 按照ICH稳定性保存条件进行相应的测试

小分子药物研发中心：生物学（Pharmacology）

肿瘤药效学评价（Oncology）

- 拥有180株肿瘤细胞，可进行抗肿瘤候选化合物的体外筛选评价，包括单药和联合用药的检测。
  - 细胞毒性检测 (WST, MTT, Trypan blue)
  - 体外联合用药检测(CalcuSyn)
- 拥有70株经过验证的体内异种移植肿瘤模型，可进行抗肿瘤药物的体内药效学研究。
- 根据项目和客户的要求进行PD研究
  - 凋亡/细胞周期检测(FCS)
  - 生物标记物分析（WB, IHC, ELISA)
  - 原代肿瘤模型、原位癌模型、转移模型、弥散模型以及同种移植模型等
  - 可进行初步小动物毒性筛选试验
  - 能够按中国SFDA和美国FDA要求为客户准备药效学部分的完整IND文件

小分子药物研发中心：质量管理与法规（QA/RA）

- 中试车间的GMP系统
  - 具有相应的质量管理系统和全职QA
  - 具有完整的质量管理文件和标准操作规程
  - 员工培训制度化
  - 将获发《药品生产许可证》
  - 质量目标
  - 化学原料药符合中/美两国I-II期临床试验用药质量标准
  - 口服制剂（片剂，胶囊剂和颗粒剂）符合中国I-II期临床试验用药质量标准
  - 按CTD Module-3的要求为客户准备药学部分的完整IND文件
    - 中文：中国SFDA；英文：美国FDA

小分子医药研发中心合作服务功能

An integrated platform covering research and translational phases

小分子医药研发中心仪器设备

以满足**FDA**及**SFDA**注册需求为目标配置了国际先进的仪器设备

已完成仪器设备投资**2000**万元
即将完成仪器设备投资**1500**万元

进口台式冻干机

高压均质机

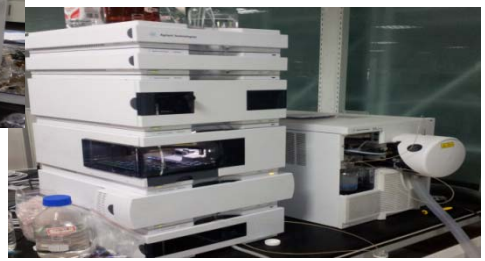
集成留样系统

实验仪器设备

ChemGlass反应釜
30-100L

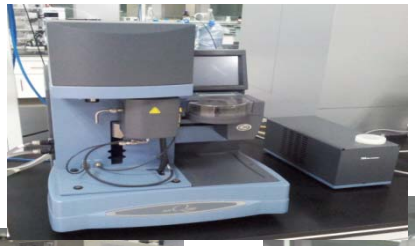
HUBER温控
-80至220度

GC-MS



LC-MS

热重分析仪



X-射线晶型分析仪

自动溶出分析仪

分析实验室

Residential District

Thank You!

mguo@ascentagepharma.com
China cell phone: 13120999418